Remarks

Reconsideration and withdrawal of the rejections of the claims, in view of the remarks herein, is respectfully requested. Claim 1 is amended. Claims 1, 3-4, 6-11, and 42-43 are pending.

Amended claim 1 is supported at page 3, lines 23-26 of the specification.

The Examiner rejected claims 1, 3-4 and 6-11 under 35 U.S.C. § 112, first paragraph, as the specification allegedly does not reasonably provide enablement for a variant or a derivative of SEQ ID NO:84 which inhibits the activity of at least one native chemokine (an enablement rejection). The Examiner also rejected claims 1, 3-4 and 6-11 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (a "written description" rejection). These rejections are respectfully traversed.

The basis for the enablement rejection is that it would require undue experimentation to make and use the claimed invention given the art-recognized unpredictability of the effect of mutations on protein function. To support the rejection, the Examiner cites to Mikayama et al. (Proc. Natl. Acad. Sci. U.S.A., 90:10056 (1993)), Voet et al. (Biochemistry, pp 126-128 and 228-234 (1990)), and Bowie et al. (Science, 247:1306 (1990)). Specifically, the Examiner asserts that Mikayama et al. and Voet et al. "demonstrate that even a single amino acid will often dramatically affect biological activity and characteristics of a protein" and that Bowie et al. teach that the positions within a protein sequence where amino acid substitution can be made with a reasonable expectation of maintaining function are limited (page 3 of the Office Action).

The claims are directed to an isolated and purified peptide, or a derivative thereof, comprising no more than 30 amino acid residues, wherein the peptide comprises residues X_1-Asp-Pro-X_2-X_3-X_4-Trp-X_5-Gln or consists of X_2-X_3-X_4 or Trp-X_5-Gln, wherein X_1 is Ala, Ile or Leu, X_2 is Lys, Ser or Thr, X_4 is Lys, Glu, Ser or Arg, X_5 is Val or Ile, and X_3 is any amino acid, and wherein the peptide inhibits the activity of at least one native chemokine.

The Examiner is requested to consider that all of the proteins in the references cited by the Examiner have at least 115 residues. Substitutions in large proteins likely alter the structure

and thus the activity of the protein. In contrast, the present claims are directed peptides of 30 residues or less.

In addition, none of the cited documents evidences that the recited amino acid substitutions in Applicant's peptides have unpredictable effects on the function of the substituted peptide.

Moreover, the Examiner has failed to consider that the claimed peptides are based on the sequence of known chemokines which are known to have biological activity. Thus, chemokines where X_1 is Ala include, for example, MCP-1, MCP-2, MCP-3, MIP1α, MIP1β, RANTES and eotaxin; where X_1 is Ile include, for example, SDF1β; or where X_1 is Leu include IL-8. Chemokines where X_2 is Lys include, for example, MCP-1, MCP-2, eotaxin, IL-8 and SDF1β; where X_2 is Ser include MIP1α, MIP1β and RANTES; or where X_2 is Thr include MCP3. Chemokines where X_4 is Lys include, for example, MCP1 and SDF1β; where X_4 is Ser include MIP1β and RANTES; where X_4 is Glu include MIP1α; or where X_4 is Arg include MCP2 and MCP3. Chemokines where X_5 is Val or Ile include, for example, MCP-1, MCP-2, and MCP-3, and SDF1α, respectively.

Further, Applicant provides data demonstrating that substitutions at positions corresponding to X_1 (from Ala to Leu), X_2 (from Lys to Ser), X_4 (from Lys to Glu) and X_5 (from Val to Ile) in a MCP-1 derived peptide (see Tables 3 and 6) did not dramatically affect the biological activity of those peptides. Thus, Applicant's specification clearly demonstrates that substitutions in a MCP-1 derived peptide did not drastically alter the activity of those substituted peptides, and so provides predictability on what alterations in a chemokine-based peptide may be made without dramatically affecting activity.

In this regard, the Examiner is also requested to consider Fox et al. (J. Med. Chem., 45:360 (2002), a copy of which is enclosed herewith). Fox et al. report the preparation of 231 variants of a chemokine peptide corresponding to SEQ ID NO:7 in the present application, and relate that almost all of the variants were active.

With regard to the undue experimentation alleged necessary to construct all possible variants and substitutions of the claimed peptides and screen for activity by examining the inhibition of all possible chemokines, the fact that the outcome of a screening program to

identify variants of a chemokine peptide with one or more activities may be unpredictable is precisely why a program is carried out. The Examiner simply cannot reasonably contend that a program to locate biomolecules with target biological or physical properties would not be carried out by the art because the results cannot be predicted in advance.

In fact, the Federal Circuit has explicitly recognized that the need, and methodologies required, to carry out extensive synthesis and screening programs to locate biomolecules with particular properties do not constitute undue experimentation. In re Wands, 8 U.S.P.Q.2d 1400, 1406-1407 (Fed. Cir. 1988), the Court stated:

> The nature of monoclonal antibody technology is that it involves screening hybridomas to determine which ones secrete antibody with desired characteristics. Practitioners of this art are prepared to screen negative hybridomas in order to find one that makes the desired antibody.

Likewise, practitioners in the art related to the present application would be well-equipped to prepare and/or screen variants of peptides with sequences in the C-terminal half of a chemokine to identify those which inhibit the activity of at least one chemokine. See also, Hybritech Inc. v. Monoclonal Antibodies Inc., 231 U.S.P.Q. 81, 84 (Fed. Cir. 1986) (evidence that screening methods used to identify characteristics [of monoclonal antibodies] were available to art convincing of enablement). Thus, the fact that a given claim may encompass a variety of molecules is not dispositive of the enablement issue, particularly in an art area in which the level of skill is very high and in which screening of large numbers of compounds has been standard practice for at least ten years (Ex parte Forman, 230 U.S.P.Q.2d 456 (Bd. App. 1986).

With respect to the written description rejection, the Examiner asserts that a) the specification and claims do not indicate what distinguishing structural or functional attributes are shared by members of the genus, b) the specification and claims do not provide guidance as to what changes should be made, and c) the specification fails to provide a representative number of species to describe the genus.

The written description requirement for a claimed genus may be satisfied through disclosure of relevant identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics sufficient to show

the application was in possession of the claimed genus. *Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1, "Written Description" Requirement*, Fed. Reg. 66, pages 1099-1111, at 1106 (2001). Moreover, satisfactory disclosure of a representative number of species depends on whether one skilled in the art would recognize that Applicant was in possession of the necessary common attributes or features of the elements possessed by members of the genus. *Guidelines for Examination of Patent Applications under the 35 U.S.C. § 112(1) Written Description Requirement*, Fed. Reg., 66, 1099 (2001).

The specification discloses that the claimed peptides are based on sequences in the C-terminal half of chemokines, and are useful to inhibit chemokine activity (page 2, line 22-page 5, line 22). Moreover, as discussed above, the specification and claims provide clear guidance as to the substitutions envisioned. Further, the claims recite structural attributes, i.e., the peptide comprises residues X_1-Asp-Pro-X_2-X_3-X_4-Trp-X_5-Gln or consists of X_2-X_3-X_4 or Trp-X_5-Gln, wherein X_1 is Ala, Ile or Leu, X_2 is Lys, Ser or Thr, X_4 is Lys, Glu, Ser or Arg, X_5 is Val or Ile, and X_3 is any amino acid, and functional attributes, i.e., the peptide inhibits the activity of at least one native chemokine, shared by members of the genus.

As Applicant envisioned the detailed structure of the claimed peptides, Applicant, at the time the above-identified application was filed, was in possession of the claimed invention.

Hence, withdrawal of the § 112(1) rejections is requested.

Conclusion

Applicant respectfully submits that the claims are in condition for allowance and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney (612) 373-6959 to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Mail Stop AF, Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 29 day of January, 2004

Gina M. Uphus _____

Name Signature